Complete Summary

GUIDELINE TITLE

Infectious complications associated with HIV infection: parasitic infections.

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Infectious complications associated with HIV infection: parasitic infections. New York (NY): New York State Department of Health; 2006 Nov. 20 p. [47 references]

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Human immunodeficiency virus (HIV)-associated parasitic infections including:

- *Pneumocystis jirovecii* pneumonia (formerly *Pneumocystis carinii* pneumonia or PCP)
- *Toxoplasma gondii* infection
- Cryptosporidiosis
- *Isospora belli* infection
- *Microsporidia species* infection
- *Cyclospora* infection
- *Giardia* infection
- Amebiasis

GUIDELINE CATEGORY

Diagnosis
Management
Prevention
Treatment

CLINICAL SPECIALTY

Allergy and Immunology
Family Practice
Infectious Diseases
Internal Medicine
Preventive Medicine

INTENDED USERS

Advanced Practice Nurses
Health Care Providers
Nurses
Physician Assistants
Physicians
Public Health Departments

GUIDELINE OBJECTIVE(S)

To provide guidelines for the diagnosis, management, and prevention of parasitic infections in human immunodeficiency virus (HIV)-infected patients

TARGET POPULATION

Human immunodeficiency virus (HIV)-infected patients with suspected or confirmed parasitic infections

INTERVENTIONS AND PRACTICES CONSIDERED

1. Management of *Pneumocystis jirovecii* pneumonia (PCP)
    - Respiratory isolation
    - Obtaining evidence of characteristic organisms in induced sputum, bronchoalveolar lavage fluid, or tissue specimen
    - Trimethoprim/sulfamethoxazole (TMP/SMX) or alternative antibiotics
    - Adding steroids and hospitalizing severely ill patients
    - Prophylaxis of PCP with TMP/SMX or alternative antibiotics
2. Management of *Toxoplasma gondii* infection
    - Imaging studies, preferably magnetic resonance imaging (MRI)
    - Using the following presumptive criteria for diagnosis: positive serum immunoglobulin G (IgG) to *T. gondii*, CD4 count <100 cell/mm^3, lack of toxoplasmosis prophylaxis
    - Brain biopsy if indicated
    - Sulfadiazine plus pyrimethamine plus leucovorin or alternative regimen
    - Prophylaxis with TMP/SMX and counseling patients to avoid sources of infection
3. Management of cryptosporidiosis

- Acid-fast staining or immunofluorescent antibody testing of the stool
- Combination of paromomycin and azithromycin
- Prevention: counseling patients to avoid contact with sources of infection

4. Management of *Isospora belli* infection
    - Acid-fast stool staining
    - TMX/SMX
    - Pyrimethamine in patients allergic to sulfa, followed by leucovorin
5. Management of *Cyclospora* infection
    - Acid-fast techniques for detection of oocysts
    - TMP/SMX followed by secondary prophylaxis with TMP/SMX
6. Management of *Giardia* infection
    - Metronidazole
    - Patient education
7. Management of amebiasis
    - Stool specimens
    - Initiation of treatment: metronidazole or tinidazole followed by paromomycin, or iodoquinol
    - For patients with E. *histolytica* infection: paromomycin, or iodoquinol, or diloxanide furoate
    - Metronidazole for extraintestinal disease

MAJOR OUTCOMES CONSIDERED

Accuracy of diagnostic tests

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

METHODS USED TO ANALYZE THE EVIDENCE

Review
Review of Published Meta-Analyses

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

AIDS Institute clinical guidelines are developed by distinguished committees of clinicians and others with extensive experience providing care to people with HIV infection. Committees* meet regularly to assess current recommendations and to write and update guidelines in accordance with newly emerging clinical and research developments.

The Committees* rely on evidence to the extent possible in formulating recommendations. When data from randomized clinical trials are not available, Committees rely on developing guidelines based on consensus, balancing the use of new information with sound clinical judgment that results in recommendations that are in the best interest of patients.

* Current committees include:

- Medical Care Criteria Committee
- Committee for the Care of Children and Adolescents with HIV Infection
- Dental Standards of Care Committee
- Mental Health Committee
- Women's Health Committee
- Substance Use Committee
- Physician's Prevention Advisory Committee
- Pharmacy Committee

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

All guidelines developed by the Committee are externally peer reviewed by at least two experts in that particular area of patient care, which ensures depth and quality of the guidelines.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

The quality of evidence (I-III) is defined at the end of the "Major Recommendations" field.

Pneumocystis jirovecii (PCP)

Presentation

Clinicians should place all hospitalized human immunodeficiency virus (HIV)-infected patients with respiratory symptoms and/or abnormal chest x-rays in respiratory isolation in a negative pressure room until active pulmonary tuberculosis is excluded or an alternative diagnosis that accounts for the abnormalities is established. (**I**)

Diagnosis

Clinicians should obtain evidence of the characteristic organisms in induced sputum, bronchoalveolar lavage fluid, or tissue specimen. (**III**)

Clinicians should obtain a bronchoalveolar lavage if induced sputum is negative or unavailable. (**III**)

Treatment

Clinicians should treat PCP with trimethoprim/sulfamethoxazole (TMP/SMX) administered either parenterally or orally, depending on the severity of the illness and likelihood of adherence. A total of 21 days of therapy should be completed. Dosing regimens and alternative drugs are listed in the table below. (**I**)

Clinicians should hospitalize patients with severe disease, as defined by initial room air pO_2 of <70 mm Hg or an arterial-alveolar oxygen gradient of >35 mm Hg, and administer parenteral treatment with the most effective agent and steroids. (**I**)

If PCP fails to improve within 7 to 10 days of treatment, clinicians should consider an alternative diagnosis and a change in PCP therapy, generally from trimethoprim/sulfamethoxazole to intravenously administered pentamidine. (**II**)

Clinicians should administer adjunctive steroids to persons with PCP who have significant hypoxia (see table below). (**I**)

Clinicians should initiate secondary prophylaxis to prevent recurrence of PCP immediately after completion of the treatment regimen. (**II**)

Table
Treatment of PCP in HIV-Infected Individuals

Clinical Status	Preferred Regimen	Alternatives
Patient acutely ill pO_2 <70 mmHg *or* A-a gradient >35 mmHg	TMP/SMX: 15 to 20 mg/kg* intravenously (IV), based on TMP, divided every 6 hours (q6h)or every 8 hours (q8h) *plus* Prednisone: 40 mg orally (PO) twice a day (bid), days 1-5 40 mg PO once a day (qd), days 6-10 20 mg PO qd, days 11-21	1. Pentamidine isethionate: 3 to 4 mg/kg/day IV, infused over 90 minutes *plus* Prednisone as in the preferred regimen *or* 2. Clindamycin: 900 mg IV q8h** *plus* Primaquine base: 15 to 30 mg PO qd *plus* Prednisone as in the preferred regimen
Patient able to take medication orally pO_2 ≥70 mmHg *or* A-a gradient ≤35 mmHg	TMP/SMX: 15 to 20 mg/kg four times a day (qid) based on weight	1. Dapsone: 100 mg PO qd*** *plus* TMP: 5 mg/kg three

Clinical Status	Preferred Regimen	Alternatives
		times a day (tid) *or* 2. Clindamycin: 450 mg PO q8h *plus* Primaquine: 15 mg base PO qd *or* 3. Atovaquone suspension: 750 mg PO bid (with a fatty meal to maximize absorption)

* The dose of 15 mg /kg is as effective as the dose of 20 mg/kg and has less hematological toxicity.
** The efficacy of clindamycin has not been established for the treatment of severe disease.
*** Check glucose-6 phosphate dehydrogenase (G6PD) screen prior to initiation. Hemolytic anemia may occur in some cases of G6PD deficiency.

Prevention

Clinicians should initiate PCP prophylaxis in patients with CD4 cell counts <200 cells/mm^3, or ≤14% of total lymphocytes, and in patients with higher CD4 counts who have a history of PCP, thrush, or unexplained constitutional symptoms of >2 weeks' duration (**I**). TMP/SMX is the referred prophylactic agent for PCP (**I**). See the table below for specific recommendations.

Clinicians should discontinue primary and secondary PCP prophylaxis when patients have responded to highly active antiretroviral therapy (HAART) with a sustained CD4 cell count of ≥200 cells/mm^3 for ≥3 months. (**I**)

Table
Prophylactic Regimens for PCP

Drug	Dose
TMP/SMX* (preferred)	1 DS tablet daily** ***or*** 1 SS tablet daily ***or*** 1 DS tablet three times/week
Dapsone***	100 mg PO qd ***or*** 50 mg PO daily ***plus*** pyrimethamine 50 mg weekly ***plus***

Drug	Dose
	leucovorin 25 mg PO weekly[#] ***or*** 200 mg ***plus*** pyrimethamine 75 mg ***plus*** leucovorin 25 mg weekly
Atovaquone¶	1500 mg PO qd (or 750 mg bid)
Pentamidine isethionate (aerosolized pentamidine)	300 mg in 6 cc sterile water via Respirgard II nebulizer once a month

DS, double strength; SS, single strength.
* There is an increased risk of prophylaxis failure with advancing immunosuppression, especially for non-TMP/SMX regimens.
** 1 DS tablet TMP/SMX is effective for prophylaxis against toxoplasmosis as well. Lower doses might also provide such protection.
*** Exclude G6PD deficiency before initiating. Hemolytic anemia may occur in some cases of G6PD deficiency.
# This regimen is effective prophylaxis against toxoplasmosis in individuals who are intolerant to TMP/SMX.
¶ Results from CPCRA/ACTG 277 showed that atovaquone in suspension, at the dose of 1500 mg PO daily is comparable to dapsone for PCP prophylaxis. No overall differences in the rate of adverse effects were noted in this study. Although some patients may better tolerate dapsone, the relative risk for discontinuation was greater with this agent than with atovaquone. Atovaquone is significantly more expensive.

Toxoplasma gondii

Diagnosis

Although the definitive diagnosis of toxoplasma encephalitis requires a brain biopsy, clinicians should use the following presumptive criteria to diagnose cerebral toxoplasmosis (**II**):

- Multiple ring-enhancing central nervous system mass lesions demonstrated by an imaging study; magnetic resonance imaging (MRI) is more sensitive than a contrast-enhanced computed tomography (CT) scan
- Positive serum immunoglobulin G (IgG) to *T. gondii*
- CD4 count <100 cells/mm^3
- Lack of toxoplasmosis prophylaxis

Clinicians should consider alternative diagnoses if there is an absence of serum IgG antibodies to *T. gondii*. (**III**)

Clinicians should obtain a brain biopsy to establish a definitive diagnosis if the patient fails to clinically and radiographically respond to therapy within 10 to 14 days or the presentation is unusual enough to make the diagnosis uncertain. (**III**)

Treatment

Clinicians should continue acute therapy for toxoplasmosis until there is clinical improvement and radiographic evidence of reduction in size and number of lesions (for 4 to 6 weeks) and should follow with suppressive therapy. (**III**)

Table
Treatment of Acute Toxoplasmosis in HIV-Infected Patients

Preferred Regimen	Alternative
Sulfadiazine 1-1.5 g PO every six hours (q6h) ***plus*** Pyrimethamine 200 mg PO loading dose followed by 50-100 mg PO qd ***plus*** Leucovorin 10-20 mg PO qd	1. Clindamycin 600-1200 mg IV every 12 hr ***plus*** Pyrimethamine 200 mg PO loading dose followed by 50-100 mg PO qd ***plus*** Leucovorin 10-20 mg PO qd ***or*** 2. Pyrimethamine 200 mg PO loading dose followed by 50-100 mg PO qd ***plus*** Leucovorin 10-20 mg PO qd ***plus*** Azithromycin 1200-1500 mg/day ***or*** Clarithromycin 500-1000 mg/day ***or*** Atovaquone 750 mg qid

Table
Prevention of Recurrent Toxoplasmosis in HIV-Infected Patients

Preferred Regimen	Alternative
Sulfadiazine 1 g PO bid ***plus*** Pyrimethamine 50 mg PO qd	1. Clindamycin 300 mg PO q6h ***plus*** Pyrimethamine 50 mg PO qd

Preferred Regimen	Alternative
plus Leucovorin 10 mg PO qd	***plus*** Leucovorin 10 mg PO qd 2. Sulfadiazine 1 g PO bid ***plus*** Pyrimethamine 50 mg PO ***plus*** Leucovorin 10 mg PO Entire regimen given thrice weekly 3. Atovaquone 750 mg bid or qid

Prevention

Clinicians should initiate prophylaxis for toxoplasmosis when a patient's CD4 count decreases to <100 cells/mm^3 and the patient is toxoplasma IgG positive (**I**). TMP/SMX is the preferred prophylactic agent for toxoplasmosis (**I**). (Refer to table below).

Clinicians should discontinue primary toxoplasmosis prophylaxis when patients have responded to HAART with a sustained (≥3 months) increase in CD4 cell count (>200 cells/mm^3). **(I**)

Clinicians should counsel HIV-infected toxoplasma-seronegative patients to avoid undercooked meats and to carefully wash hands after handling cat litter boxes and after gardening. (**III**)

Table
Toxoplasmosis Prophylaxis Regimens in HIV-Infected Patients

Medication	Dose
TMP/SMX	1 DS PO daily (preferred) ***or*** 1 SS PO daily
Dapsone* ***plus*** Pyrimethamine ***plus*** Leucovorin	50 mg PO daily 50 mg PO weekly 25 mg PO weekly
Dapsone* ***plus***	200 mg weekly

Medication	Dose
Pyrimethamine ***plus*** Leucovorin	75 mg weekly 25 mg weekly
Atovaquone	1500 mg once a day

DS, double strength; SS, single strength.
* Exclude G6PD deficiency before initiating.

Cryptosporidiosis

Presentation

Clinicians should include cryptosporidiosis in the differential diagnosis of diarrhea, especially large-volume diarrhea. (**I**)

Diagnosis

Clinicians should specifically request acid-fast staining or immunofluorescent antibody testing of the stool to establish a diagnosis of cryptosporidiosis. (**I**)

Clinicians should specifically alert the laboratory to look for cryptosporidia if this diagnosis is suspected (**III**).

Treatment

Clinicians should prescribe a combination of paromomycin 1 g twice a day (bid) plus azithromycin 600 mg orally (PO) daily for 4 weeks, followed by paromomycin maintenance therapy. (**III**)

Prevention

Clinicians should counsel patients to:

- Avoid contact with human and animal feces, pets with diarrhea, dogs or cats <6 months of age
- Avoid drinking water from lakes, streams, or rivers, unless it has been adequately boiled
- Boil water for 1 minute when public health agencies issue a boil-water advisory during waterborne outbreaks of cryptosporidiosis

Isospora belli

Diagnosis

Because *Isospora belli* is shed intermittently in the stool, clinicians should request multiple stool specimens for modified acid-fast stool staining. (**I**)

Treatment

Clinicians should treat *Isospora belli* with TMP/SMX double strength (DS) PO four times daily for at least 10 days. (**I**)

Clinicians should consider using pyrimethamine 50 to 75 mg/day for 10 days in patients allergic to sulfa, followed by leucovorin 5 to 10 mg/day. (**III**)

Clinicians should consider discontinuing isosporiasis prophylaxis for patients who are asymptomatic and have sustained CD4 >200 cells/mm^3 for ≥3 months. (**III**)

Cyclospora

Diagnosis

Clinicians should base the diagnosis of cyclosporiasis on microscopic detection of oocysts in stool. (**I**)

Treatment

Clinicians should prescribe oral TMP/SMX 160 mg/800 mg four times a day for 10 days, followed by secondary prophylaxis with TMP/SMX three times a week to treat *Cyclospora* infection in HIV-infected patients. (**I**)

Giardia

Treatment

Clinicians should treat *Giardia* with metronidazole 250 mg PO three times a day (tid) for 5 to 10 days. (**I**)

Clinicians should educate *Giardia*-infected patients regarding improved hygienic measures. (**III**)

Amebiasis

Diagnosis

Clinicians should obtain at least three stool specimens before excluding the diagnosis of amebiasis. (**II**)

Treatment

Clinicians should initiate treatment of *Entamoeba histolytica* when trophozoites with ingested red blood cells are present in the stool. One of the following regimens should be used (**II**):

- Metronidazole 750 mg tid for 10 days or 2.4 g daily (qd) for 3 days
- Tinidazole 2 g PO qd for 3 days followed by paromomycin 500 mg tid for 7 days
- Iodoquinol 650 mg tid for 20 days

Clinicians should treat patients with asymptomatic *E. histolytica* infection with one of the following regimens (**II**):

- Paromomycin 500 mg tid for 7 days
- Iodoquinol 650 mg tid for 20 days
- Diloxanide furoate 500 mg tid for 10 days

Clinicians should treat extraintestinal disease with metronidazole 750 mg tid for 10 days or 2.4 g qd for 3 days (**II**).

Definitions:

Quality of Evidence for Recommendation

I. Evidence from one or more properly randomized, controlled trial
II. Evidence from one or more well-designed clinical trial without randomization; from cohort or case-controlled studies
III. Evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is classified for selected recommendations (see "Major Recommendations").

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate diagnosis, management and prevention of parasitic infections

POTENTIAL HARMS

Adverse Effects of Medications

Adverse effects associated with trimethoprim/sulfamethoxazole (TMP/SMX) include cytopenias, rash, increased serum liver enzymes, hyperkalemia, interstitial nephritis, nausea, vomiting, and fever.

Refer to Table 2 in the original guideline document for information on toxicities associated with clindamycin, dapsone, pentamidine and other antibiotics.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

The AIDS Institute's Office of the Medical Director directly oversees the development, publication, dissemination and implementation of clinical practice guidelines, in collaboration with The Johns Hopkins University, Division of Infectious Diseases. These guidelines address the medical management of adults, adolescents and children with HIV infection; primary and secondary prevention in medical settings; and include informational brochures for care providers and the public.

Guidelines Dissemination

Guidelines are disseminated to clinicians, support service providers and consumers through mass mailings and numerous AIDS Institute-sponsored educational programs. Distribution methods include the HIV Clinical Resource website, the Clinical Education Initiative, the AIDS Educational Training Centers (AETC) and the HIV/AIDS Materials Initiative. Printed copies of clinical guidelines are available for order from the NYSDOH Distribution Center for providers who lack internet access.

Guidelines Implementation

The HIV Clinical Guidelines Program works with other programs in the AIDS Institute to promote adoption of guidelines. Clinicians, for example, are targeted through the Clinical Education Initiative (CEI) and the AIDS Education and Training Centers (AETC). The CEI provides tailored educational programming on site for health care providers on important topics in HIV care, including those addressed by the HIV Clinical Guidelines Program. The AETC provides conferences, grand rounds and other programs that cover topics contained in AIDS Institute guidelines.

Support service providers are targeted through the HIV Education and Training initiative which provides training on important HIV topics to non-physician health and human services providers. Education is carried out across the State as well as through video conferencing and audio conferencing.

The HIV Clinical Guidelines Program also works in a coordinated manner with the HIV Quality of Care Program to promote implementation of HIV guidelines in New York State. By developing quality indicators based on the guidelines, the AIDS Institute has created a mechanism for measurement of performance that allows providers and consumers to know to what extent specific guidelines have been implemented.

Finally, best practices booklets are developed through the HIV Clinical Guidelines Program. These contain practical solutions to common problems related to access, delivery or coordination of care, in an effort to ensure that HIV guidelines are implemented and that patients receive the highest level of HIV care possible.

IMPLEMENTATION TOOLS

Personal Digital Assistant (PDA) Downloads

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness
Timeliness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

New York State Department of Health. Infectious complications associated with HIV infection: parasitic infections. New York (NY): New York State Department of Health; 2006 Nov. 20 p. [47 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2006 Nov

GUIDELINE DEVELOPER(S)

New York State Department of Health - State/Local Government Agency [U.S.]

SOURCE(S) OF FUNDING

New York State Department of Health

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Not stated

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the New York State Department of Health AIDS Institute Web site.

AVAILABILITY OF COMPANION DOCUMENTS

This guideline is available as a Personal Digital Assistant (PDA) download from the New York State Department of Health AIDS Institute Web site.

PATIENT RESOURCES

None available

NGC STATUS

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